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| 10/575,592 | 04/12/2006 | Anthony Kettle | 1012501PUS | 9563 |

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| EXAMINER | |
|---|---|
| BERCH, MARK L | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/575,592 | KETTLE ET AL. | |
| | Examiner | Art Unit | |
| | /Mark L. Berch/ | 1624 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *11-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *02/11/2008,07/24/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 11-19, are rejected under 35 U.S.C. 102(b) as being anticipated by 6025361

See Column 5, first, second, 4th, 5th, 6th, 8th, 9th, and 14th (last) species. See example 12, species b), d) and e). These all have R1=R2=alkyl, R4 = alkyl.

With regard to claim 20, note use of P2S5 in e.g. examples 1-3.

With regard to claim 17, page 12 states that the compounds are used for assorted inflammatory disorders, and the reference also has inflammatory disorders. For example, rhinitis appears at specification, page 12, line 26, and in the reference, column 4, line 58. The reference lists atopic diseases; page 12 has asthma, perhaps the most common atopic disease, as well as dermatitis. Also, the reference has dementia; page 12 has Alzheimer's Disease, the most common form of dementia.

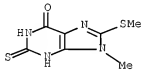
Claims 11-15 are rejected under 35 U.S.C. 102(b) as being anticipated by EP 430300, Reichman, Dietz et al.

In EP 430300, See compounds 15-17, corresponding to X=S, Y=O or vice versa R3=H, R1=R2=methyl, R4 = alkylthio.

In Reichman, see compounds 24, 25 and 26 of similar structure.

In Dietz et al, see Formula I and Formula II. Note Table 1, species 2-7, and others, Table 2, 52-57, Table 3, 72-77. All have R4 as alkylthio.

In Cook, see Compound X:




The examiner has reviewed 11577833, 11720913 but there is no conflict.

***Double Patenting***

Claims 11-20 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims of copending Application No. 11756967. Although the conflicting claims are not identical, they are not patentably distinct from each other because there is no line of patentable demarcation. 11756967 has R1=H, R2=alkoxy-alkyl, which fall within claim 1 of 10575592. The sole difference is that R4 in 10575592 is methyl, but in 11756967 is it H. This is not a patentable distinction,a s these are homologues, see ***Ex parte Fischer***, 96 USPQ 345; ***In re Zickendraht***, 138 USPQ 22; ***in re Bowers and Orr***, 149 USPQ 570. Note that in the latter case, the filing of the terminal disclaimer resolved the issue.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact

terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 20 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Several problems arise:

A. The scope of the ortho ester cannot be deemed enabled. The simplest orthoester is formic acid orthoester. This will not give a claim 1 product, as it would yield R4=H, not permitted.

B. The same is true for "alpha-halo-substituted carboxylic acid". This would xover something like 1-Cl-cyclohexanecarboxilic acid.

C. The second converting option is not enabled. This would cover converting e.g. a R1=methyl compound to R1=ethyl. How would that be done?

Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15's "for use as" is a mental step, a statement of intention, and does not limit the claim. If applicants actually intend a method or composition, the claim must be re-written.

Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The scope of claim 17 is unknown. There is no generally accepted list of disorders that would define this category. Some examples are listed in the specification, but this is not presented as definitive list, and indeed, it includes such diverse disorders such as Alzheimer's disease, gingivitis, sepsis, and lung cancer.

Claims 18-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 18-19 provides for the use of the compounds for preparing medicinal compositions, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 18-19 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35

U.S.C. 101. See for example ***Ex parte Dunki***, 153 USPQ 678 (Bd.App. 1967) and ***Clinical Products, Ltd.*** v. ***Brenner***, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim 17 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Pursuant to ***In re Wands***, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), one considers the following factors to determine whether undue experimentation is required: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. Some experimentation is not fatal; the issue is whether the amount of experimentation is "undue"; see ***In re Vaeck***, 20 USPQ2d 1438, 1444.
The analysis is as follows:
(1) Breadth of claims.

(a) Scope of the compounds. Owing to the scope of the four primary variables, especially R2, millions of compounds are embraced.

(b) Scope of the diseases covered. As noted above, the scope of the claim is unknown. The analysis below is based on what appears in the specification, page 12.
I. "Inflammatory diseases or conditions" The scope of treating inflammation generally is extraordinarily broad. Inflammation is a process which can take place in virtually any part of the body. There is a vast range of forms that it can take, causes for the problem, and

biochemical pathways that mediate the inflammatory reaction. It is one of the most pervasive of all body processes. Inflammation is a very general term which encompasses a huge variety of specific processes.

Inflammation is the reaction of vascularized tissue to local injury; it is the name given to the stereotyped ways tissues respond to noxious stimuli. These occur in two fundamentally different types. Acute inflammation is the response to recent or continuing injury. The principal features are dilatation and leaking of vessels, and recruitment of circulating neutrophils. Chronic inflammation or "late-phase inflammation" is a response to prolonged problems, orchestrated by T-helper lymphocytes. It may feature recruitment and activation of T- and B-lymphocytes, macrophages, eosinophils, and/or fibroblasts. The hallmark of chronic inflammation is infiltration of tissue with mononuclear inflammatory cells. Mechanistically, chronic inflammation encompasses a broad spectrum of immunologic processes, including antibody formation, antibody-dependent cell-mediated cytotoxicity, and cell-mediated immunity (delayed-type hypersensitivity). Granulomas are seen in certain chronic inflammation situations. They are clusters of macrophages which have stuck tightly together, typically to wall something off. Granulomas can form with foreign bodies such as aspirated food, toxocara, silicone injections, and splinters.

Otitis media is an inflammation of the lining of the middle ear and is commonly caused by Streptococcus pneumoniae and Haemophilus influenzae.

Cystitis is any inflammation of the bladder, often caused by bacteria. Two ordinary types are eosinophilic and tuberculous cystitis. Interstitial cystitis (IC) is a particularly severe form, an inflammation of the bladder wall which may include Glomerulations. The origins and mechanism are largely unknown, and it isn't even clear whether there is just

one form of the disease or several. There is no actual pharmaceutical treatment for the disease itself, although a few drugs can give some relief of symptoms, specifically Elmiron and DMSO.

Blepharitis is a chronic inflammation of the eyelids that is caused by a staphylococcus. Dacryocystitis is inflammation of the tear sac, and usually occurs after a long-term obstruction of the nasolacrimal duct and is caused by staphylococci or streptococci. Preseptal cellulitis is inflammation of the tissues around the eye, and Orbital cellulitis is an inflammatory process involving the layer of tissue that separates the eye itself from the eyelid. These life-threatening infections usually arise from staphylococcus. Hence, these types of inflammations are treated with antibiotics.

There is also a wide assortment of forms of conjunctivitis, including seasonal allergic conjunctivitis, perennial allergic conjunctivitis, giant papillary conjunctivitis (GPC) (a chronic yet poorly condition associated with contact lens wear), Vernal keratoconjunctivitis and atopic keratoconjunctivitis. In addition to types of allergic conjunctivitis there is also bacterial conjunctivitis (e.g. from Streptococcus pneumoniae, Haemophilus influenzae, and Staphylococcus aureus) and viral conjunctivitis (e.g. from gonorrhea, herpes simplex, chlamydia, adenoviruses or enteroviruses) Parasitic conjunctivitis (e.g. from ***Onchocerca volvulus***, ***Loa loa***, ***Wuchereria bancrofti*** or ***Trichinella spiralis)***, fungal conjunctivitis (e.g. from ***Candida albicans*** or ***Sporothrix schenckii)***, Phlyctenular Conjunctivitis, Inclusion Conjunctivitis, immunologic conjunctivitis, irritant conjunctivitis (e.g. from burns, chlorine or air pollutants ), Radiation conjunctivitis, and assorted forms of neonatal conjunctivitis (which can be caused by e.g. a blocked tear duct).

Cholecystitis is gallbladder inflammation usually caused by a gallstone that cannot pass through the cystic duct. In those cases, it normally cannot be treated by pharmaceuticals but instead the gallbladder is removed. Cholecystitis without the formation of gallstones, called acalculous cholecystitis, is caused by bacteria such as Salmonella, Staphylococcus, Streptococcus (as part of scarlet fever), and leptospirosis, and thus may be treatable by treating the underlying infectious agent. Acute inflammation of the gall bladder can also arise from typhoid; treatment is with antibiotics.

The term "arthritis" is used for any of the dozens of kinds of inflammation of the joints arising from a wide diversity of causes and mediators, many of which are unknown. It mostly commonly refers to any of osteoarthritis, gouty arthritis, or rheumatoid arthritis. These are three totally different and unrelated disorders, which all have "arthritis" in their name and involve inflammation of the joints. Rheumatoid arthritis is an inflammatory disorder causing destruction of articular cartilage, in which macrophages accumulate in the rheumatoid synovial membrane. Mediators are cytokines, including IL-1, IL-18, TNF-I and IFN-K. It is thus an autoimmune condition where the body's immune system attacks its joints. In gouty arthritis, joint inflammation is caused by the formation of monosodium urate monohydrate (MSU) crystals within the joint space. Acute attacks of gout are treated with colchicine (to inhibit of MSU-induced chemotactic factor release by PMNs) and after the acute phase with allopurinol to control the blood levels of uric acid. Osteoarthritis is a degenerative cartilage disorder; cartilage breakdown causes bones to rub against each other. Causes include injuries, diseases such as Paget's disease, and long term obesity, but often the cause is unknown, and the full mechanism has not been discovered. It is treated with NSAIDs and COX-2 inhibitors. Complicating matters further is that fibromyalgia is

sometimes also intended to be included in the loose term "arthritis". There is also Psoriatic Arthritis (including DIP, and spondylitis) which is believed to be autoimmune in origin but is a separate disorder from RA. There are also an assortment of infectious arthritis, i.e. arthritis caused by bacteria, rickettsiae, mycoplasmas, viruses (or vaccinations given to prevent viral infections), fungi, or parasites. Included in this category are various types of septic arthritis and mycotic arthritis, and viral arthritis, such as rubella arthritis, Lyme arthritis (caused by a spirochete transmitted by a tick), Mumps arthritis, arboviral arthritis, syphilitic arthritis, parvovirus arthritis, tuberculous arthritis, Varicella arthritis, gonococcal arthritis, rubella arthritis, Reiter's syndrome (which includes a form of arthritis commonly arising from infection by Chlamydia trachomatis) etc. These assorted disorders can arise from quite varied sources. Thus, in addition to the above, CPDD, sometimes called pseudoosteoarthritis, or pseudogout, arises from Calcium Pyrophosphate Deposition. It is treated with nonsteroidal anti-inflammatory drugs , corticosteroids and Colchicine. Menopausal arthritis is due to ovarian hormonal deficiency. Neuropathic arthritis (which comes in several forms, such as Charcot's disease) can arise from sources as diverse as Diabetes Mellitus, Steroid treatment, Leprosy, Chronic alcoholism, Heavy metal poisoning and Neoplastic peripheral neuropathy. Arthritis can also arise from injury to the supporting ligaments or other structures contained within or associated with the joint, a condition often called post-traumatic arthritis. Juvenile Dermatomyositis (JDMS) is an inflammatory disease of unknown cause that affects the skin, muscle and the gastrointestinal tract. Polymyalgia Rheumatica (PMR) causes severe stiffness, aching and pain in the neck, shoulders, upper arms, lower back, hips or thighs. Polymyositis is due to inflammation of skeletal muscle, resulting in weakness.

Sinusitis is the inflammation of the mucosal lining of one or more of the 4 cavities near the nasal passages (ethmoid, maxillary, frontal, and sphenoid sinuses). It commonly accompanies upper respiratory viral infections which obstruct the opening, but such obstruction can also arise from abnormalities in the structure of the nose, enlarged adenoids, diving/swimming, infections from a tooth, trauma to the nose, and foreign objects that are stuck in the nose. Bacteria, notably Streptococcus pneumonia, Haemophilus influenza, and Moraxella catarrhalis grown in the trapped secretions. In most cases it requires no treatment, but antibiotics may be given, along with acetaminophen for pain and nosedrops, for relief of symptoms.

Pharyngitis is infection and inflammation of the throat (including the nasopharynx, uvula, and soft palate)and tonsillitis is of the tonsils. These are caused by a variety of viruses (adenoviruses, influenza viruses, parainfluenza viruses, Epstein-Barr virus, enteroviruses, Herpes simplex virus), mycoplasmas (e.g. Mycoplasma pneumoniae), and bacteria (Group A Beta Hemolytic Streptococci (GABHS), Streptococcus pyogenes, Neisseria Gonorrhea, Hemophilus Influenza Type B) as well as fungal infections, parasitic infections, cigarette smoke, and unknown causes.

Similarly, Osteomyelitis is the inflammation of bones, often caused by bacteria (most commonly Staphylococcus Aureus), and sometimes by fungi or viruses. Chronic Recurrent Multifocal Osteomyelitis (CRMO), a chronic inflammatory disease of unknown etiology, results in recurrent fever and the development of multiple inflammatory bone lesions.

Dacryoadenitis, an inflammation of the tear gland, can arise from infectious mononucleosis, mumps, gonorrhea, or influenza.

Pneumonia is an inflammation of the lungs. Lobar pneumonia affects one or more sections (lobes) of the lungs. Bronchial pneumonia (or bronchopneumonia) affects patches throughout both lungs. Bacterial pneumonia is caused by various bacteria notably Streptococcus pneumoniae. Viral pneumonia is caused by viruses (such as respiratory syncytial, parainfluenza, and influenza), Other causes are fungi, mycoplasmas, rickettsias (especially Q fever), Chlamydia, or parasites. It can also occur as a hypersensitivity, or allergic response, to agents such as mold, humidifiers, and animal excreta, and in such a case would be treated with anti-allergic agents. Treatment may include antibiotics for bacterial pneumonia. Antibiotics may also speed recovery from mycoplasma pneumonia and some special cases. There is no clearly effective treatment for viral pneumonia.

Adult (or Acute) Respiratory Distress Syndrome (ARDS) is severe inflammation in both lungs resulting in an inability of the lungs to function properly. ARDS is a devastating, often fatal, inflammatory lung condition that usually occurs in conjunction with catastrophic medical conditions, such as pneumonia, shock, sepsis, and trauma. No specific therapies currently exist for ARDS patients. Treatment primarily involves supportive care in an intensive care unit , including use of a mechanical ventilator and supplemental oxygen to help patients breathe.

Chronic bronchitis is a long-term inflammation of the bronchi, which results in increased production of mucus, as well as other changes. Chronic bronchitis has no specific organism recognized as the cause of the disease. Cigarette smoking is cited as the most common contributor to chronic bronchitis, followed by bacterial or viral infections and environmental pollution. Treatment is purely supportive and may include bronchodilators

for inhaled medications, oxygen supplementation, lung reduction surgery and lung transplantation.

Chronic Obstructive Pulmonary Disease (COPD) is a slowly progressive disease of the airways that is characterized by a gradual loss of lung function. COPD includes chronic obstructive Bronchitis (which involves inflammation and eventual scarring of the bronchi) and emphysema (enlargement and destruction of the alveoli). Emphysema comes in several forms, including Congenital Lobar Emphysema, Bullous Emphysema, Centrilobular Emphysema (Proximal acinar emphysema), Panacinar (panlobular), Distal acinar (paraseptal) as well as Alpha-1 antitrypsin (AAT) deficiency, which is the genetic form of emphysema; patients often have both a form of bronchitis and emphysema. Ordinary chronic bronchitis is sometimes included with COPD even if there is no actual obstruction, and asthmatic bronchitis is generally included in COPD as well. Persons with COPD typically develop smaller air passageways, which can become clogged with mucus and have partially destroyed alveoli. There is no pharmaceutical treatment for COPD per se. Instead, treatment is supportive and designed to relieve symptoms and improve quality of life. Thus, oxygen is often given to partially compensate for the loss of lung function. Bronchodilators can expand passageways in the lungs, Corticosteroids can reduce inflammation and Antibiotics can ward off bacterial infections, but none of these treat the COPD itself.

Acute bronchitis is the inflammation of mucous membranes of the bronchial tubes and is usually caused by infectious agents such as bacteria or viruses. It may also be caused by physical or chemical agents -- dusts, allergens, strong fumes -- and those from chemical cleaning compounds, or tobacco smoke. (Acute asthmatic bronchitis may happen as the

result of an asthma attack, or it may be the cause of an asthma attack.) Acute bronchitis is usually a mild, and self-limiting condition, with complete healing and return to function. Most of the treatment is supportive of the symptoms, and may include analgesics, such as acetaminophen for fever and discomfort.

Asthma is a chronic, inflammatory lung disease involving recurrent breathing problems. It is characterized by three airway problems: obstruction, inflammation, and hyper-responsiveness. These lead to contraction of airway muscles, mucus production, and swelling in the airways. There are many different asthma triggers.

Myocarditis is an inflammation of the muscular middle layer of the heart (myocardium) Viruses, bacteria, and noninfectious diseases can cause it. Treatment is primarily supportive e.g. drugs may be used to improve the heart's ability to contract and to remove extra fluids from the body. Unless the underlying infectious agent itself is treatable, this inflammation is not itself treated.

Mucocutaneous lymph node syndrome (MLNS) or Kawasaki syndrome is a potentially fatal inflammatory disease that affects the heart, circulatory system, mucous membranes, skin, and immune system. Its cause is unknown.

Glossitis is inflammation of the tongue. Local causes of glossitis include bacterial or viral infection, mechanical irritation or injury from burns, rough edges of teeth or dental and oral appliances, or other trauma; exposure to irritants (tobacco, alcohol, hot foods, or spices), and sensitization (to e.g. toothpaste, mouthwash, breath fresheners, dyes in candy, plastic in dentures or retainers) anemia and other B vitamin deficiencies, erythema multiform, pemphigus vulgaris, syphilis, and other disorders. It can be inherited. Corticosteroids such as prednisone may be given to reduce the inflammation. Antibiotics,

antifungal medications, or other antimicrobials may be prescribed if the cause of glossitis is an infection. Anemia and nutritional deficiencies must be treated, often by dietary changes or other supplements.

Meningitis is the inflammation of the meninges—the surrounding 3-layered membranes of the brain and spinal cord, and the fluid it is bathed in, (CSF). It can be caused by virtually any known infectious agent. Thus, if it is caused by Haemophilus influenzae or Neisseria meningitis, the antibiotic derivative rifampin would be used.

Myelitis is inflammation of the spinal cord.

Dactylitis is an inflammatory affection of the fingers.

Inclusion body myositis in an inflammatory slowly progressive proximal myopathy which may cause dysphagia and mild to moderate muscle wasting. Steroids and immunosuppression have generally been generally ineffective. Its pathogenesis is unknown, but ubiquitin, prion protein, and tau protein has been found in these inclusions.

Behçet's disease is a syndrome of unknown origin, but appears to be an autoimmune disorder. It is characterized primarily by inflammation of the blood vessels. Symptoms include a broad range of problems, which include mouth sores, genital sores, skin sores or lesions, meningoencephalitis, Uveitis, inflammation of the joints, thrombophlebitis, aneurysms, digestive tract ulceration (sometimes called Behçet's colitis)

Encephalitis is inflammation of the brain itself, often caused by a group of arboviruses. Treatment of encephalitis is largely supportive because no specific antiviral agents, except for that which works against herpes simplex virus, are available for therapy.

Inflammation in the brain is a significant component of some important neurodegenerative conditions, including Alzheimer's Disease, AIDS dementia, Pick's Disease, Parkinson's Disease, and Huntington's Disease. The circumstances here are poorly understood because while there does not appear to be lympho-infiltrative processes, there is neuropathological evidence for immune activation. Thus, inflammation may be a disease-aggravating or even a disease-ameliorating factor in pathogenesis, or a non-contributory consequence of the injurious cascade of neurodegeneration and thus incidental.

Hepatitis is an inflammation of the liver, usually caused by viral invasion, notably hepatitis A, B and C, but sometimes Epstein-Barr virus; herpes simplex viruses; measles, mumps, and chicken pox viruses; and cytomegaloviruses. Treatment, when possible, is with antivirals. Inflammation of the liver also take the form of alcoholic hepatitis. Lupoid hepatitis is an autoimmune disorder.

Hemorrhoids is an enlarged or varicose condition of the hemorrhoidal veins and tissues around the anus, either internal or external. Anything which obstructs the free circulation of the blood in the portal system will give rise to hemorrhoids. Constipation, straining at stool, diarrhea, dysentery, rough toilet paper, uncleanliness, pelvic tumors, displacement of the uterus and pregnancy are among the most common causes.

There is a series of inflammatory problems directly connected to neutrophil-endothelial cell adhesion (NECA). These include frostbite injury, bacterial meningitis, acute airway inflammation, allograft rejection, hemorrhagic shock, septic shock, ischemia and reperfusion injuries.

Urethritis is an inflammation of the duct that leads from the bladder to the body's exterior. It is often due to fecal contamination or irritation due to physical or chemical

substances (e.g. introduction of foreign bodies into the urethra, bubble bath, or soap) or gonorrhea. Treatment may simply involve the withdrawal of the offending chemical agent, or the administration of antibiotics, when Neisseria gonorrhoeae is involved.

Inflammation can arise from the eruption of teeth in a child (teething).

Inflammation of the nails can arise from chronic paronychia, fungus (especially Candida albicans), trauma, impaired circulation, and dermatitis.

Bright's disease (or glomerulonephritis) is inflammation of the glomeruli and the nephrons, the structures in the kidney that produce urine. It usually results from an infection, such as a streptococcal infection, that occurs somewhere else in the body. There is no real treatment beyond relief of the symptoms.

Thyroiditis is an inflammation of the thyroid gland, and takes three forms. Hashimoto's Thyroiditis (chronic lymphocytic thyroiditis) is the most common type of thyroiditis. It is an autoimmune disorder, and treatment is to start thyroid hormone replacement. For De Quervain's Thyroiditis (subacute or granulomatous thyroiditis), treatment is usually bed rest and aspirin to reduce inflammation. Occasionally cortisone and thyroid hormone may be used. Silent Thyroiditis usually arises following pregnancy. Treatment is usually bed rest with beta blockers.

Regional enteritis (Crohn's disease or ileitis) is an autoimmune disorder which is associated with the presence of Mycobacterium paratuberculosis. It can affect any part of the gastrointestinal tract but most commonly affects the ileum. The inflammation is controlled primarily by regulation of diet, antibiotics if abscesses and fistulas are present, sometimes Prednisone and other corticosteroids, and surgery.

Another category of inflammatory disorders is Interstitial lung disease, or ILD, (interstitial pulmonary fibrosis), a term that includes more than 180 chronic lung disorders, which may be chronic, nonmalignant (non-cancerous) and noninfectious. Interstitial lung diseases are named after the tissue between the air sacs of the lungs called the interstitium -- the tissue affected by fibrosis (scarring). The common link between the many forms of ILD is that they all begin with an inflammation. The three main kinds are bronchiolitis - inflammation that involves the bronchioles (small airways); alveolitis - inflammation that involves the alveoli (air sacs); and vasculitis - inflammation that involves the small blood vessels (capillaries). More than 80 percent of interstitial lung diseases are diagnosed as pneumoconiosis, a drug-induced disease, or hypersensitivity pneumonitis. An important group of the ILDs are the Idiopathic interstitial pneumonias including idiopathic pulmonary fibrosis (IPF), nonspecific interstitial pneumonia, cryptogenic organizing pneumonia, acute interstitial pneumonia, Respiratory bronchiolitis-associated interstitial lung disease, desquamative interstitial pneumonia and lymphoid interstitial pneumonia. Other ILDs are bronchiolitis obliterans, histiocytosis X, chronic eosinophilic pneumonia, granulomatous vasculitis, Goodpasture's syndrome and pulmonary alveolar proteinosis. The cause of interstitial lung disease is not known, however, a major contributing factor is thought to be inhaling environmental pollutants. Other contributing factors include Sarcoidosis, certain drugs, radiation, connective tissue or collagen diseases and family history. Treatments may include corticosteroids, influenza or pneumococcal pneumonia vaccine but these are of limited effectiveness.

Many Occupational Lung Diseases are inflammatory in origin, arising from repeated and long-term exposure to certain irritants on the job. These include for example

asbestosis, coal worker's pneumoconiosis (caused by inhaling coal dust), silicosis (caused by inhaling free crystalline silica), byssinosis (caused by dust from hemp, flax, and cotton processing, also known as brown lung disease), aluminosis, anthracosis ("collier's lung", from the accumulation of carbon from inhaled smoke or coal dust in the lungs), chalicosis (stone-cutters' lung disease, due to inhaling stone dust), siderosis (occurring in iron workers, produced by the inhalation of particles of iron), tabacosis, hypersensitivity pneumonitis (caused by the inhalation of fungus spores from moldy hay, bird droppings, and other organic dusts and occupational asthma (caused by inhaling certain irritants in the workplace, such as dusts, gases, fumes, and vapors).

Proctitis is a form of inflammation of the rectum, and includes Antibiotic-Induced Proctitis, Gonorrheal Proctitis, Herpetic Proctitis, Ischemic Proctitis, Radiation Proctitis, Syphilitic Proctitis and idiopathic proctitis.

Pulmonary Sarcoidosis causes small lumps, or granulomas, which generally heal and disappear on their own. However, for those granulomas that do not heal, the tissue can remain inflamed and become scarred, or fibrotic. Pulmonary sarcoidosis can develop into pulmonary fibrosis. Bronchiectasis, a lung disease in which pockets form in the air tubes of the lung and become sites for infection, can also occur. Treatment may include the use of corticosteroids.

Stomatitis, inflammation of the mouth, and mucositis, inflammation of the mucosa can arise from sources as diverse as Candida albicans, dentures, chemotherapy and radiation therapy to the head, neck or mouth ("Radiation mucositis"). It may be secondary to infection, trauma, systemic diseases or autoimmune mechanisms. These come in many forms, such as aphthous ulcers, Acute Necrotizing Ulcerative Gingivitis i.e. "trench mouth",

and Lichen Planus. Herpetiform ulcers treatment has ranged from antibiotics, immunosuppressants and yogurt, to Lactobacillus capsules, tetracycline and systemic steroids. Palliative measures include topical anesthetics, Vitamin E, analgesics, and coating agents. Antiviral agents may be used if viral origin is established.

Rhinitis is a reaction that occurs in the eyes, nose and throat when airborne irritants (allergens) trigger the release of histamine. Histamine causes inflammation and fluid production in the fragile linings of nasal passages, sinuses, and eyelids. The two categories of rhinitis are allergic rhinitis (seasonal and perennial) and nonallergic Rhinitis (including eosinophilic, rhinitis medicamentosa, vasomotor Rhinitis, neutrophilic rhinosinusitis, and others), which come from fumes, odors, temperature or atmospheric changes, smoke, etc. Treatments for nonallergic rhinitis include oral medications, inhaled medications, immunotherapy, and surgery for some conditions. Wegener's Granulomatosis is a disease that usually begins as a localized granulomatous inflammation of upper or lower respiratory tract mucosa and may progress into generalized necrotizing granulomatous vasculitis and glomerulonephritis. The cause is unknown. Although the disease resembles an infectious process, no causative agent has been isolated. Treatment is with immunosuppressive cytotoxic drugs.

Pancreatitis is inflammation of the pancreas and can arise from abdominal trauma, or the formation of gallstones that obstruct the common bile duct. It can be associated with excessive ingestion of alcohol; with disorders such as cystic fibrosis or Reye's syndrome; or with scorpion stings. Infectious causes include mycoplasmas, Epstein-Barr viruses, Coxsackie viruses, leptospirosis, hepatitis viruses, mumps, congenital German measles,

Ascaris worms, and syphilis. The inflammation per se is generally not treatable. Treatment is usually supportive and consists of the management of pain and intravenous feeding.

Neuroretinitis is a type of inflammation of the retina and optic nerve of the eye ("optic neuritis"). It is often idiopathic. It frequently arises secondary to some kind of infection, such as Hepatitis B, HSV, EBV, influenza A, mumps, Coxsackie B, TB, salmonella, Lyme disease, syphilis, leptospirosis, Histoplasmosis, Toxoplasmosis, toxocara, Sarcoidosis and cat-scratch disease. Treatment is thus to the underlying cause. For example, Diffuse unilateral subacute neuroretinitis (DUSN) arises from nematodes deep in the retina or in the subretinal space. Anthelminthic treatment is then used. When the origin is Toxoplasmosis, then anti-Toxoplasma medications such as Pyrimethamine. Vogt-Koyanagi-Harada syndrome (Harada's disease) is an acute inflammatory, immune-mediated disorder that can cause choroidal neovascularization, severe chorioretinal atrophy, and secondary glaucoma.

River blindness arises from inflammation of the eye caused by larvae (microfilaria) of the nematode ***Onchocerca volvulus***, although the ***Wolbachia*** bacteria may be involved as well.

Multifocal choroiditis and panuveitis (MCP) is a posterior chorioretinal inflammatory disease of unknown etiology

There ar also other forms of choroiditis, inflammation of the middle coat (choroid) of the eyeball, as well as uveitis, which is inflammation of the parts of the eyes that make up the iris. Other eye inflammations include scleritis and episcleritis, inflammation of tissues on the sclera.

Gastritis is inflammation to the stomach lining. Atrophic gastritis is characterized by the loss of the stomach cells that are responsible for manufacturing acid, pepsin, and intrinsic factor. This condition occurs in older people or those suffering from Helicobacter pylori. Erosive (hemorrhagic) gastritis occurs when shallow ulcers or sores develop on the upper layer of the stomach lining, usually because of the excessive ingestion of a stomach irritant such as aspirin or alcohol.

There can also be mentioned appendicitis, which can occur when a hard piece of stool blocks the opening of the appendix, causing swelling and inflammation.

The great majority of skin problems involve some type of inflammation, such as response to physical injury (e.g. sunburn, ticks, abrasion, or a bee string), acute allergic contact dermatitis (such as poison ivy), and infections (such as boils and cold sores). Ingrowing hairs, or pili incarnati, can cause acute pustular reactions. Cancerous lesions of the skin frequently show some degree of inflammatory response. Acne's inflammation is caused by leakage of sebum and keratin debris outside the distended pilosebaceous duct. The bacillus Propionibacterium acnes, which populates the lesions, may also contribute indirectly to this inflammation by metabolizing the sebum to produce irritant fatty acids. Inflammation in skin problems is usually the result of the release of chemical mediators in the skin, notably histamine, peptides (kinins) and fatty acids (prostaglandins and leukotrienes), which are formed enzymatically in response to e.g. injury. Medications designed to counteract inflammation in the skin may or may not antagonize the effects of the particular type of mediator involved, if that is known. The inflammation can take many different forms, including redness, (from dilation of blood vessels); heat, (from increased blood flow); swelling (from leakage of fluid from the small blood vessels); whealing reactions

(hives, nettle rash, urticaria) in which vascular changes predominate, and pain or itching. Blisters (from enzymes released from inflammatory cells, resident cells of the skin, or blood plasma components) can cause the breakdown of proteins responsible for the structural integrity of the skin, leading to serious inflammatory disorders such as pemphigus. In addition, the affected skin may feel indurated (hardened) because of the deposition of the coagulation protein fibrin and the infiltration by inflammatory blood cells (lymphocytes, histiocytes, and polymorphonuclear leukocytes).

Prostatitis, inflammation of the prostate, comes in several different forms, including those of bacterial origins, and those which are not, including chronic abacterial prostatitis and asymptomatic inflammatory prostatitis. Certain types of anti-inflammatory agents, such as non-steroidal anti-inflammatory medications (Ibuprofen and naproxen) along with muscle relaxants can be used in the non-bacterial cases.

There are a number of different forms of vasculitis, including Churg-Strauss vasculitis, consecutive vasculitis, granulomatous vasculitis of central nervous system, hypersensitivity vasculitis, (called also allergic or leukocytoclastic vasculitis or leukocytoclastic angiitis which arises from hypersensitivity to an antigenic stimulus), hypocomplementemic vasculitis, isolated vasculitis of central nervous system, nodular vasculitis, overlap vasculitis (polyangiitis overlap syndrome), pulmonary vasculitis including Wegener's granulomatosis, rheumatoid vasculitis, segmented hyalinizing vasculitis (livedo vasculitis), Polyarteritis nodosa, and urticarial vasculitis. There are also specific forms of arteritis, including coronary arteritis, equine viral arteritis, giant cell arteritis (cranial, granulomatous, or temporal arteritis or Horton's disease), infantile arteritis, infectious arteritis, arteritis obliterans (endarteritis obliterans), rheumatic

arteritis, syphilitic arteritis, Takayasu's arteritis (aortic arch, or brachiocephalic arteritis or Martorell's syndrome or pulseless disease; it is of unknown origin), tuberculous arteritis, endarteritis obliterans, and verminous mesenteric arteritis.

Cystic fibrosis (CF) is an inherited disease characterized by an abnormality in the glands that produce sweat and mucus. It is chronic, progressive, and is usually fatal. The basis for the problem with CF lies in an abnormal gene, which results in an atypical electrolyte transport system within the cells of the body. The abnormal transport system causes the cells in the respiratory system, especially the lungs, to absorb too much sodium and water. This causes the normal thin secretions in our lungs to become very thick and hard to remove. The high risk of infection in the respiratory system leads to damage in the lungs, lung that do not work properly, and eventually death of the cells in the lungs. The most common causes for infection in the lungs are Staphylococcus aureus, Haemophilus influenza and Pseudomonas aeruginosa (PA). The disorder itself is largely untreatable.

Osgood-Schlatter disease is a common form of inflammation of the knee in active adolescents. It has no pharmaceutical treatment per se. Other inflammations of the knee include Sinding-Larsen-Johansson disease, Patellofemoral syndrome, and osteochondritis dissecans.

Adhesive capsulitis is a type of inflammation of the shoulder. Its origin is usually unknown.

There can be a generalized inflammatory response of the entire body. When it arises from a proven source of infection, it is called sepsis. When it does not, it is called systemic inflammatory response syndrome (SIRS). Both of these are characterized by extensive cytokine dysregulation.

The above list is by no means complete, but demonstrates the extraordinary breadth of causes, mechanisms and treatment (or lack thereof) for inflammation. It should be noted that determining that a disorder is an inflammatory one is sometimes not an easy manner. For example, it has taken decades of research to discover that the destruction of the central area of the retina, which is the hallmark of age-related macular degeneration, actually arises out of an inflammatory process, involving the Complement Pathway. This only became well established in 2005. It is entirely possible that a majority of disorders presented considered idiopathic --- including many untreatable disorders --- are in fact inflammatory disorders.

It must be noted that an inflammatory response is a normal body process and for good reason. A certain level of inflammatory response is needed to protect the body from invading organisms, especially bacteria, viruses, and parasites. An acute inflammatory response is needed to activate the healing process for burns, mediated by a range of MMPs. In sprains or other ligament injuries, some inflammatory response is needed initially to initiate repair of the damage. In mechanical wounds, some inflammatory response is required for satisfactory wound healing and indeed anti-inflammatory drugs such as cortisone can impair healing when administered at the time of wounding. In fact, inflammation is too important to be dependent on a single pathway and so inflammation can be initiated by numerous different systems, and generally, if one fails or is thwarted, another can do some or all of the job.

II. Stroke. There are two fundamentally different types, ischemic (due to interruption of the blood supply) and hemorrhagic (due to rupture of a blood vessel or an abnormal vascular structure).

III. Alzheimer's disease, a form of dementia, which is a taupathy.

IV. Parkinson's disease, which is characterized by the degeneration and death of dopamine-producing cells in the substantia nigra, located in the midbrain, along with the presence of cytoplasmic protein inclusions called Lewy bodies.

V. Amyotrophic lateral sclerosis, a disease characterized by the degeneration of motor neurons.

VI. Lung Cancer. The main types of lung and pleural cancer are small cell (i.e. oat cell, including combined oat cell), adenocarcinomas, Bronchioloalveolar carcinomas (Nonmucinous, Mucinous, and Mixed mucinous and nonmucinous or indeterminate cell type), Acinar, Papillary carcinoma, Solid adenocarcinoma with mucin, Adenocarcinoma with mixed subtypes, Well-differentiated fetal adenocarcinoma, Mucinous (colloid) adenocarcinoma, Mucinous cystadenocarcinoma, Signet ring adenocarcinoma, and Clear cell adenocarcinoma), squamous cell (Papillary, Clear cell, Small cell and Basaloid), mesothelioma (including epithelioid, sarcomatoid, desmoplastic and biphasic) and Large Cell Carcinoma (which include Large-cell neuroendocrine carcinoma, Combined large-cell neuroendocrine carcinoma, Basaloid carcinoma, Clear cell carcinoma Lymphoepithelioma-like carcinoma, and Large-cell carcinoma with rhabdoid phenotype). In addition there are also the carcinomas with pleomorphic, sarcomatoid or sarcomatous elements, including Carcinomas with spindle and/or giant cells, Spindle cell carcinoma, Carcinosarcoma and Pulmonary blastoma. The non-small cell lung carcinomas also include Adenosquamous carcinoma, the Carcinoid tumor (both typical Carcinoid and atypical Carcinoid) as well as carcinomas of salivary-gland type, including mucoepidermoid carcinoma and adenoid cystic

carcinoma. There are some soft tissue tumors including localized fibrous tumor (formerly called benign fibrous mesothelioma); epithelioid haemangioendothelioma; pleuropulmonary blastoma (which occurs three fairly different substituted-types); chondroma; calcifying fibrous pseudotumor of the visceral pleura); congenital peribronchial myofibroblastic tumors, diffuse pulmonary lymphangiomyomatosis and desmoplastic round cell tumor. There are assorted bronchial adenomas (e.g. adenoid cystic carcinomas, mucoepidermoid carcinomas, mucous gland adenomas, and oncocytomatous bronchial mucous gland adenoma) as well as other adenomas, including papillary adenoma. There are some papillomas, including squamous cell papilloma and glandular papilloma. There is also malignant melanoma of the lung, Hamartoma, cylindroma (cylindroadenoma), some germ cell tumors, thymoma and sclerosing haemangioma and many others as well. Lung cancers are quite diverse. Thus, for example, oat cell carcinoma, Signet ring adenocarcinoma, pleuropulmonary blastoma, cylindroma, and malignant mesothelioma really have very little in common, other than being cancers of the lung.

(2) The nature of the invention and predictability in the art: The invention is directed toward the treatment of disease and is therefore physiological in nature. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See ***In re Fisher***, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(3) Direction or Guidance: That provided is very limited. The dosage information that is provided at page 13, line 14 is generic, that is, it is not linked to any specific disease, and is extremely broad (2000-fold range).

(4) State of the Prior Art: These compounds are thio or dithioxanthines with a specific substitution pattern in the 8-position. So far as the examiner is aware, no thio or dithioxanthines with any substitution pattern in the 8-position have been used for the treatment of e.g. Alzheimer's Disease or stroke or atherosclerosis, etc.

(5) Working Examples: There are none to the treatment of any disease or any animal model.

(6) Skill of those in the art: One of ordinary skill in the art knows that there is no common mechanism by which all, or even most, inflammations arise. Mediators include bradykinin, serotonin, histamine, fibrin, some PDE4 isoenzymes, kallikrein, plasmin, thrombin, PAF, Mac-1, VLA-4, VLA-5, VLA-6, VCAM-1, LFA-1, ICAM-1, Prostaglandins and cyclic endoperoxides (particularly prostacycline, prostaglandin E2, and thromboxane A2), leukotrienes (especially LTB4, LTC4, LTD4, and LTE4) and cytokines, and many, others. Examples of pro-inflammatory cytokines include IL-1-alpha, IL-1beta, IL-6, IL-8, IL-11, IL-12, IL-17, IL-18, GM-CSF, CNTF, OSM (Oncostatin M), MCP-1, CCL5 (RANTES), TGF-beta, ENA-78, Osteopontin, Cyclophilin A, LIF (leukemia inhibitory factor), leptin, MIP-1, TWEAK, MGSA, keratinocyte-derived chemokine, PF4, MCP-1 (GDCF), IFN-gamma, TNF-α, Abscisic acid, high mobility group box chromosomal protein 1 (HMGB-1), S100A12 (EN-RAGE), TRAIL, sCD40L, IL-19, IL-20, IL-21, IL-22, IL-23, IL-24, IL-25, IL-26, IL-27, IL-32, and IL-33. The Complement Pathway, which exists in two separate branches, uses C1, C4a, C4b, C2, C3a, C3b, C5a, C5b, C6, C7, C8 and C9, as well as the membrane attack complex

(MAC) and other complexes, C3 and C5 convertase enzymes, PI3K-gamma, Magnesium ions, and Factors B, D, F, H, etc.

One of ordinary skill in the art also knows that mediation of inflammation is among the most pervasive and complex of all body process. There are very complex interactions among just the cytokines. As a second example, the Hageman factor is a protein that initiates three different processes: a) the intrinsic clotting process which operates via thrombin and fibrin, b) the fibrinolytic system which produces fibrinolysis via plasmin and 3) the kallikrein/kinin cascade, which produces the kinins, e.g. bradykinin. Further, Plasmin can also activate C3 and C5 in the complement cascade (an entirely separate set of vascular events) producing C3a and C5a, respectively, as can thrombin.

One of ordinary skill in the art also knows that there are many paradoxical features in the inflammation system. As an example, in lung inflammation, nitric oxide appears to be a pro-inflammatory mediator in acute situations e.g. ARDS but anti-inflammatory in more stable situations. As a second example, the cytokine TGF-beta-1 possesses both pro-inflammatory and anti-inflammatory activities. Virtually all cells have TGF-beta-1 receptors, and the cytokine has many other roles other than in inflammation. As a third example, CRF appears to have both pro-inflammatory and anti-inflammatory activities.

And in fact, there is a tremendous diversity in the combination of mechanisms that produce inflammation For example, Atherosclerosis arises from the accumulation of macrophage white blood cells and is promoted by low density (especially small particle) lipoproteins. Very few, if any, other inflammatory disorders have this particular mechanism.

Thus, one of ordinary skill in the art knows that, treatments for inflammation are normally tailored to the particular type of inflammation present, as there is no, and there can be no "magic bullet" against inflammation generally.

For a compound or genus to be effective against inflammation generally is contrary to the present understanding of medical science. Thus, it is not reasonable for any agent to be able to treat inflammation generally. That is, the skill is so low that no compound effective generally against inflammatory disorders has ever been found. In terms of the individual inflammatory disorders, this is completely varied. It ranges from areas where the skill level is high, as in asthma, to ARDS, where the skill level is so low that there is no effective pharmacological treatment.

What very few treatments that the massive research effort on Alzheimer's Disease has produced are means of providing Acetylcholinesterase inhibition, (Aricept®, Cognex®, Exelon®, and Reminyl®), or voltage-dependent NMDA-antagonists (Memantine), properties that the claimed compounds are not disclosed to have.

The only types of drugs found effective for stroke have been clot-busters, and these are not relevant for hemorrhagic stroke. Again, this is a different mode of action.

ALS is a virtually untreatable disease. Riluzole, approved in 1996, is as of 2008 the sole FDA approved drug for the disease. The mechanism of action, a glutamate regulator, is unrelated to the mode of action here. Even as of 2007, the toxin that kills motor neurons --- assuming that this is what is occurring --- has not even been identified.

Parkinson's disease is considered untreatable. Some symptomatic relief is available through drugs which increase the amount of dopamine, again, a different mechanism.

(7) The quantity of experimentation needed: Owing to the factors listed above, especially in points 1(b), 4 and (6), experimentation needed will be extensive. Because of the sheer scope of this claim language, dozens of unrelated diseases will have to be tested. Many of these are already known to be resistant to pharmacological treatment as noted above.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. ***In re Wright***, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

***Specification***

Page 15, line 11 should say "published", not "copending".

Any inquiry concerning this communication or earlier communications from the examiner should be directed to /Mark L. Berch/ whose telephone number is 571-272-0663. The examiner can normally be reached on M-F 7:15 - 3:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on (571)272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Mark L. Berch/
Primary Examiner
Art Unit 1624

3/5/2009